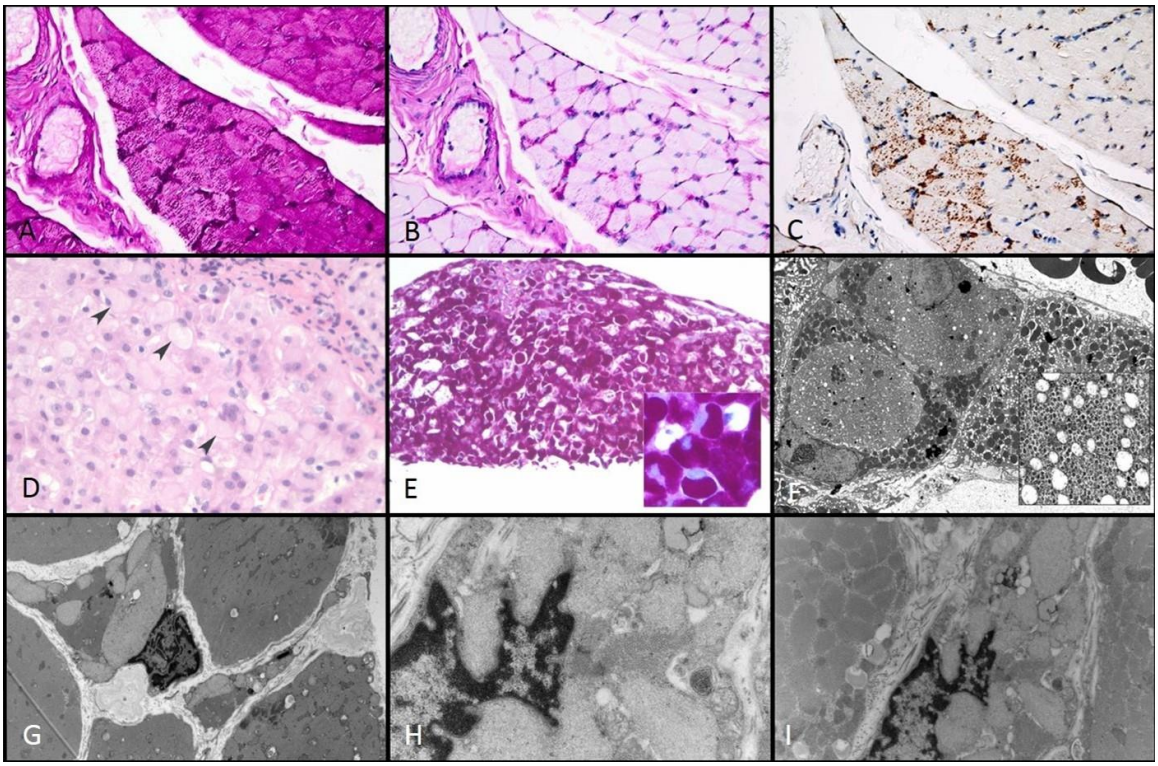
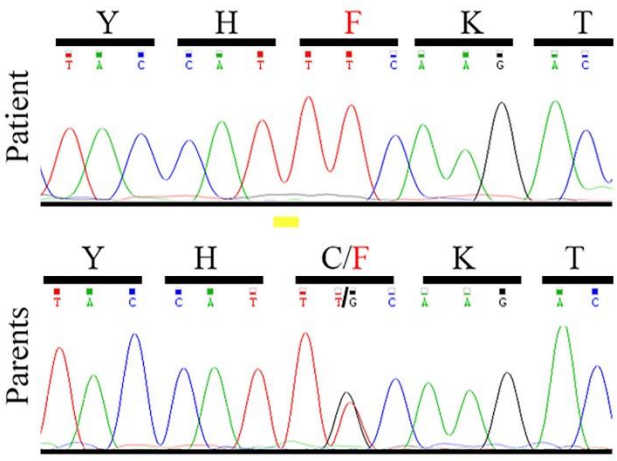


Endocardial biopsy (A-D): almost all cardiomyocytes are vacuolated (A: H&E, 100x), containing PAS-positive material (B) incompletely digested by alpha-amylase (C). The accumulated material was positively stained with ubiquitin antibody (D). Skeletal muscle biopsy: approximately 15% of the myofibers are vacuolated, containing PAS-positive material (E, toluidine blue-PAS, 200x). Liver biopsy (F, G): The liver light microscopically demonstrates pale acidophilic cytoplasmic inclusions (arrowheads) within hepatocytes (F, H&E, 400x). PAS stain demonstrates cytoplasmic inclusions (G, PAS, 200x) displacing hepatocyte nuclei (inset, 600x). Transmission electron micrographs (H-K) revealed cytoplasmic accumulation of abnormal filamentous material intermixed with glycogen granules in hepatocytes (H, 4000x) and myofibers (I and J, 3,000x and 20,000x).A higher magnification (K, 200,000x) shows finely filamentous elements of the accumulated polyglucosan in a myocyte.

A



B

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364 RSAFSYHF-KTPDCKGW 379 Patient
364 RSAFSYHC-KTPDCKGW 379 Homo sapience
364 RSTLSYHC-KTPDCRGW 379 Rattus norvegicus
369 RSENSYHC-KTPDCAGW 384 Danio rerio
442 RSPNSFHC-KTTDCRGW 458 Falco peregrinus
118 ----SYHC-RTADCRGW 130 Xenopus tropicalis
1381--AF--HC-KTPDCPGW1393 Apis mellifera
100 -SAFTYHC--S-ECK-- 110 Arabidopsis thaliana
266 QNYFPFVCAKCPRCKKW 282 Wickerhamomyces ciferrii
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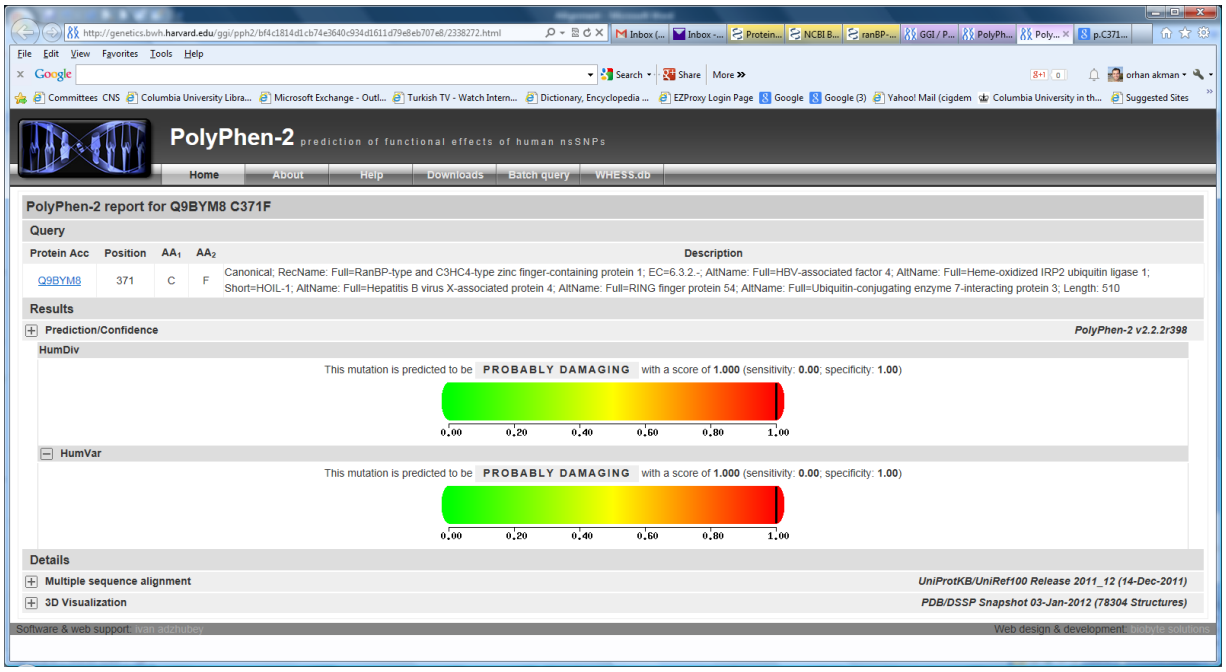
C



The mutation, NP_112506.2:p.Cys371Phe, has changed the amino acid cysteine to phenyl alanine in 371st codon. Father and mother were heterozygous for this change and the patient was homozygous (A). Amino acid cysteine has been conserved among species (B). PolyPhen has found this change deleterious for protein function* (C).

*http://genetics.bwh.harvard.edu/ggi/pph2/7b3ce4caa2df2ee995752960382af7dbb7d0e605/4261999.html